Figure 1/6

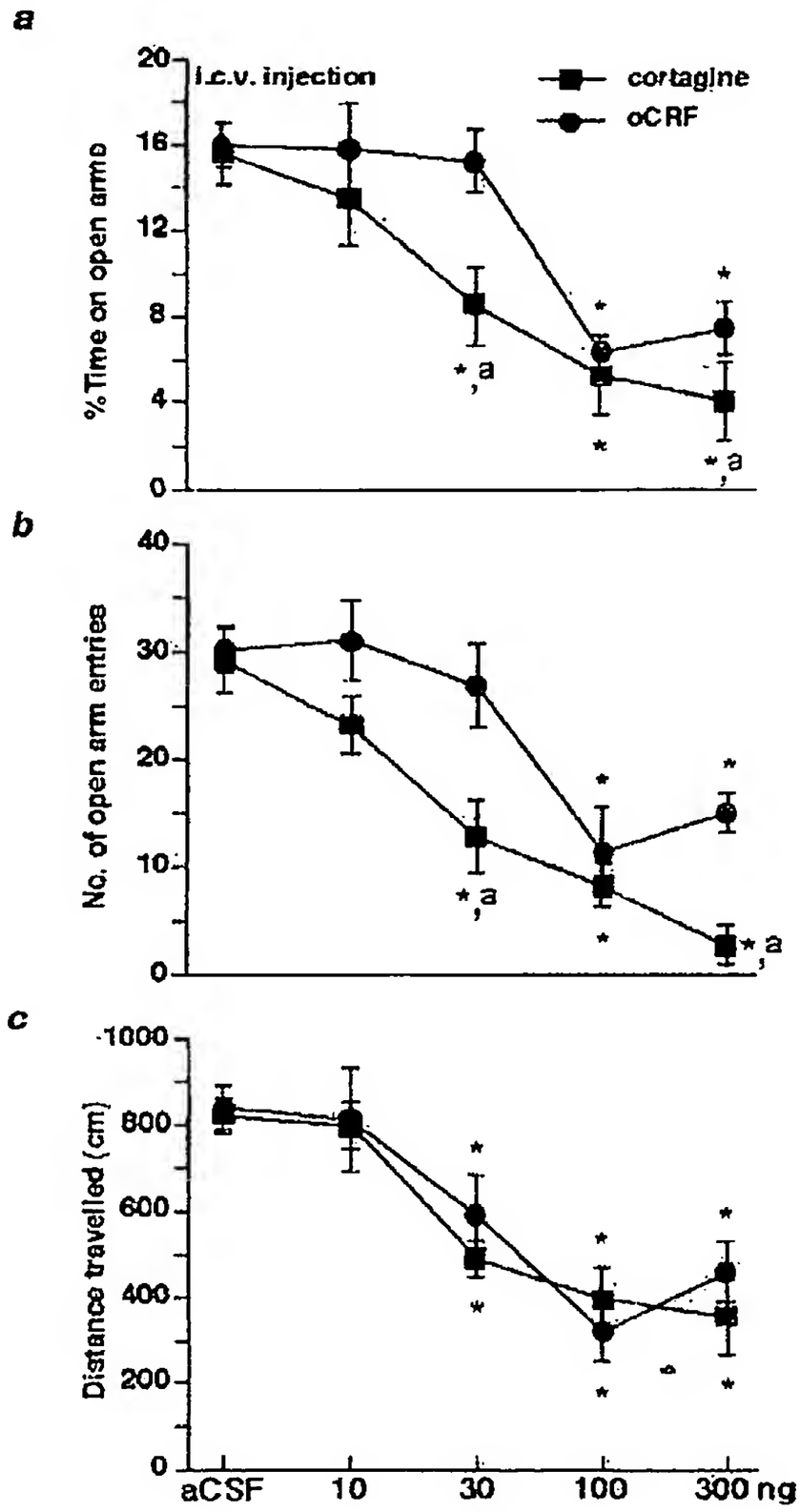

Figure 2/6

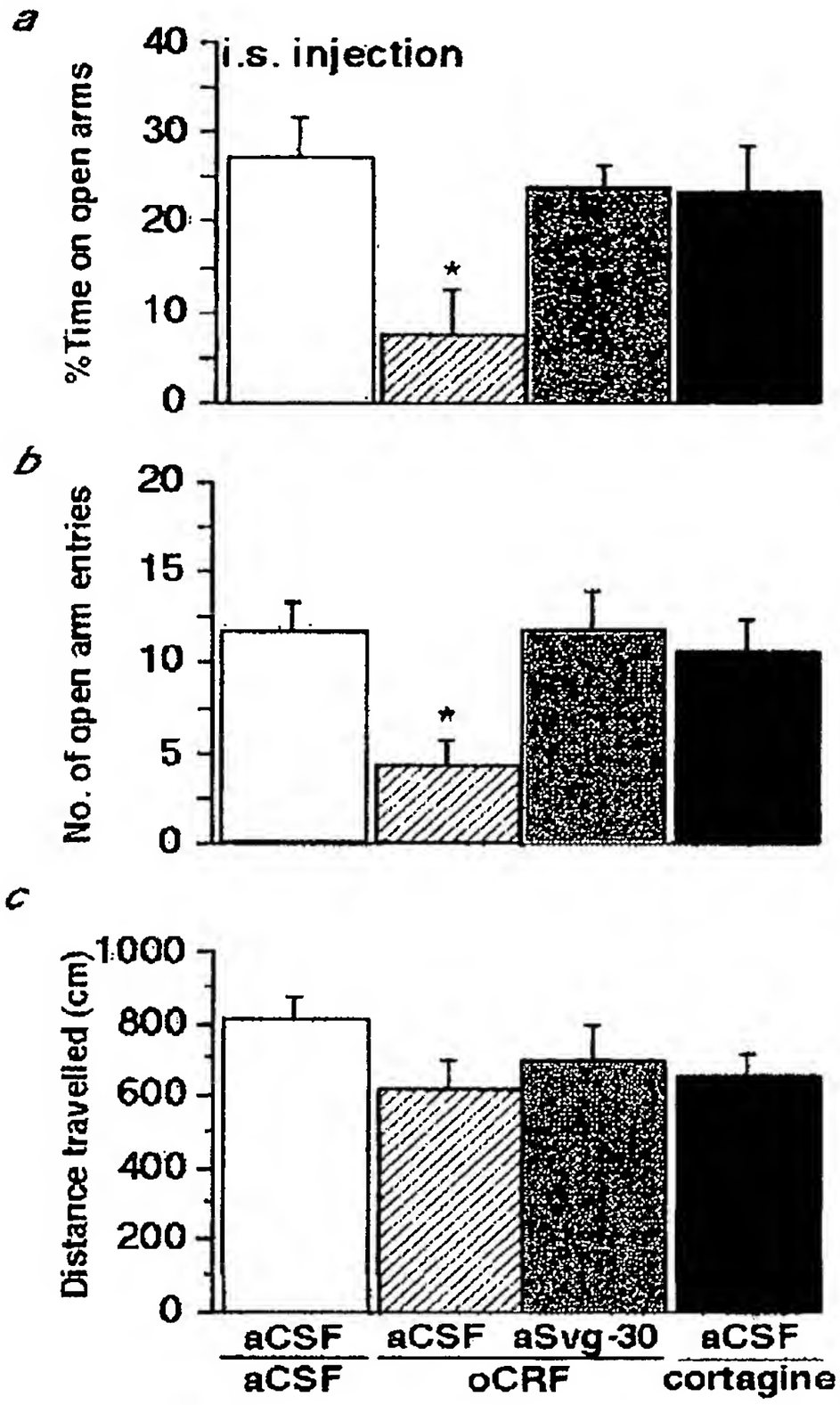

Figure 3/6

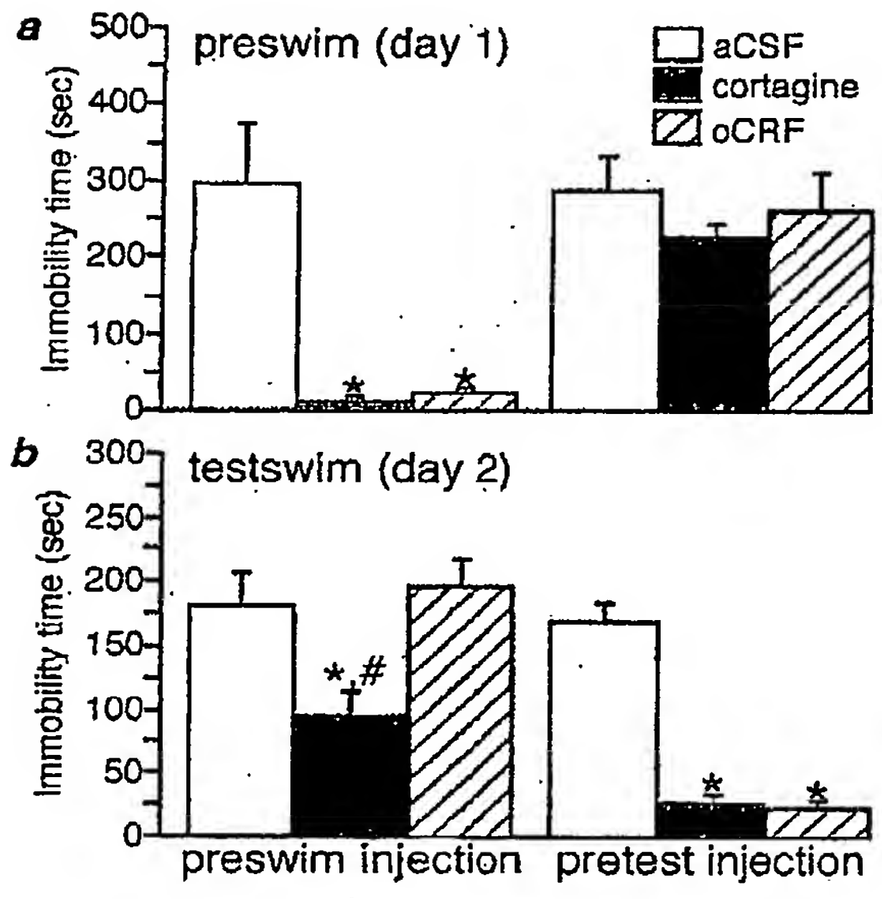

Figure 4/6

Table 1. Sequence alignment of oCRF, h/rCRF, Svg and their chimeric analogs

No.	Peptide	Sequence
1	$oCRF^{1-41}$	SQEPPISLDL TFHLLREVLE MTRADQLAQQ AHSNRKLLDI A
2	$h/rCRF^{1-41}$	SEEPPISLDL TFHLLREVLE MARAEQLAQQ AHSNRKLMEI I
3	Svg^{1-40}	*ZGPPISIDL SLELLRKMIE IEKQEKEKQQ AANNRLLLDT I*
4	$[h/rCRF^{1-13}]x[Svg^{13-29}]x[h/rCRF^{31-41}]$	SEEPPISLDL TFHLLRKMIE IEKQEKEKQQ AHSNRKLMEI I
5	$[h/rCRF^{1-30}]x[Svg^{30-40}]$	SEEPPISLDL TFHLLREVLE MARAEQLAQQ *AANNRLLLDT I*
6	$[Svg^{1-12}]x[h/rCRF^{14-30}]x[Svg^{30-40}]$	*ZGPPISIDL SLELLREVLE MARAEQLAQQ AANNRLLLDT I*
7	$[Svg^{1-29}]x[h/rCRF^{31-41}]$	*ZGPPISIDL SLELLRKMIE IEKQEKEKQQ* AHSNRKLMEI I
8	$[Ala^{40}][Svg^{1-12}]x[h/rCRF^{14-30}]x[Svg^{30-39}]$	*ZGPPISIDL SLELLREVLE MARAEQLAQQ AANNRLLLDT* A
9*	$[Glu^{21}, Ala^{40}][Svg^{1-12}]x[h/rCRF^{14-30}]x[Svg^{30-39}]$	*ZGPPISIDL SLELLREVLE MERAEQLAQQ AANNRLLLDT* A

The three main building blocks of the chimeric peptides, the N-terminal, central and C-terminal domains, are indicated. Sequences derived from h/rCRF, Svg, and oCRF are underlayed in grey, black and white, respectively. Z, pyroglutamic acid.
* Compound 9 is cortagine.

Figure 5/6

Table 2. Binding affinites of oCRF, h/rCRF, Svg and their chimeric analogs

Compound	IC_{50}, nM		
	rCRFR1	mCRFR2β	rCRFBP[#]
1	1.8 (1.1-2.4)	160 (120-200)	450 (420-480)
2[†]	1.6 (1.3-1.9)	42 (25-59)	0.54 (0.38-0.71)
3[†]	0.52 (0.29-0.74)	0.9 (0.72-1.1)	57 (45-70)
4	0.47 (0.18-0.77)	0.69 (0.45-0.93)	ND
5	2.0 (0.80-3.1)	330 (140-530)	ND
6	9.5 (4.8-14)	700 (490-910)	ND
7	1.8 (0.75-2.8)	0.98 (0.59-1.4)	ND
8	1.8 (1.4-2.1)	400 (360-450)	1.9 (1.8-2.0)
9[*]	2.6 (1.6-3.4)	540 (480-590)	> 1000

IC_{50} values are the mean of at least four experiments performed in duplicate. 95 % confidence intervals are given in parentheses. Compound 2-7 were dissolved in 10 mM aqueous acetic acid, whereas compound 1, 8, and 9 were dissolved in phosphate buffered saline (see Results section for details). ND, not determined.

[#] The intermediate compounds of the agonist development were not tested for their affinity to rCRFBP.

[†] Binding data taken from Eckart et al., 2001.

[*] Compound 9 is cortagine.

Table 3. Comparison of the pharmacological and physicochemical properties of cortagine and oCRF

Peptide	Biological potency EC_{50}, nM		c_{max}, µM	p*I*-value*
	rCRFR1	mCRFR2β		
cortagine	0.18 (0.10-0.26)	16 (11-20)	> 1000	4.8
oCRF	0.47 (0.14-0.80)	8.8 (6.0-12)	> 1000	6.4

IC_{50} and EC_{50}values are the mean of at least four experiments performed in duplicate. 95 % confidence intervals are given in parentheses.
* Isoelectric points were determined by IEF.